



NOTES

CHROMOSOMAL DELETION SYNDROMES

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- **Congenital syndromes:** genetic deletions during parental gamete formation
- **Mutation:** permanent DNA change

TYPES

Numerical

- Entire chromosome deletion (aneuploidy)

Structural

- Structural change due to chromosome break → separated portion rearrangement
 - **Balanced rearrangement:** without genetic material gain/loss; not associated with phenotypic anomaly
 - **Unbalanced rearrangement:** with genetic material gain/loss; associated with phenotypic anomaly
- **Deletion size:** proportional to clinical severity

CAUSES

- Chromosomal breakage mechanism
 - **Endogenous:** defect in DNA replication, transcription, recombination, repair
 - **Exogenous:** radiation, chemical substances → DNA damage

RISK FACTORS

- Parental genetic defect

COMPLICATIONS

- Congenital heart defect; recurrent infection (e.g. urinary tract infections, otitis media); gastrointestinal abnormalities; severe constipation; impaired development; intellectual disability

SIGNS & SYMPTOMS

- Atypical facial features, short stature, noise sensitivity, additional organ defect-related signs/symptoms

DIAGNOSIS

- History, clinical examination

LAB RESULTS

- Genetic tests
 - e.g. karyotyping, fluorescent in-situ hybridization (FISH)

TREATMENT

OTHER INTERVENTIONS

- Early intervention education
- Physical, language, occupational therapy
- Associated condition treatment

VISIT...

LANZAROTE
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CRI DU CHAT SYNDROME

osms.it/cri-du-chat

PATHOLOGY & CAUSES

- **Chromosomal deletion syndrome:** physical, neurological congenital anomalies
 - Caused by partial/total **macrodeletion in short arm of chromosome 5 (5p-)**
 - AKA cat cry syndrome, 5p- syndrome, Lejeune's syndrome
 - **Cri-du-chat:** "cat's cry"
- **Inheritance pattern:** mostly sporadic
 - **Paternal origin (most):** sporadic chromosome breakage during male gamete formation
 - **Inherited Cri du chat syndrome (rare):** parent with balanced translocation → child with unbalanced translocation (rearrangement with genetic material loss) in 5p
- Most due to terminal deletions

CAUSES

- **Deletion**
 - **5p15.2:** major clinical features (e.g. dysmorphism, intellectual impairment)
 - **5p15.3:** altered larynx anatomy, central nervous system (CNS) dysfunction → cat-like cry, high-pitched voice, speech delay
- **CTNND2 gene loss:** severe mental disability

RISK FACTORS

- Parental genetic defect
- Biologically-female individuals (more common)

COMPLICATIONS

- Low birth weight; postnatal failure to thrive; **microcephaly**; developmental, **mental disability**; pneumonia; congenital **heart defects**; craniofacial dysmorphism; respiratory distress syndrome; hydrocephalus; chronic otitis media;

gastrointestinal/genitourinary abnormalities

SIGNS & SYMPTOMS

- **Cat-like cry, high-pitched voice:** may resolve during infancy
- **Poor feeding**
- **Facial features:** microretrognathia (hypoplastic, posteriorly displaced mandible); round face; **epicanthus** (prominent eye folds); downslanting eyelids; hypertelorism (widely-spaced eyes); wide nasal bridge; low-set ears
 - Physical signs become less prominent with age
- **Body features:** muscular hypotonia, short stature, short neck, small hands, single palmar crease, scoliosis, prenatal-growth deficiency, low birth weight
- **Ocular:** myopia, strabismus, cataracts
- **Neurologic:** noise sensitivity (hyperacusis); behavior alterations (e.g. aggression, hyperactivity, repetitive movement)
- **Adulthood:** small testes, premature hair graying (age ≥ 15), constipation
 - Physical signs become less prominent with age

DIAGNOSIS

LAB RESULTS

- **Cytogenetic tests:** FISH, karyotyping, chromosomal analysis
- **Molecular genetics tests:** heteroduplex analysis; single strand conformation analysis; whole genome sequencing; Southern, northern blotting



Figure 22.1 The facial appearance of a child with Cri du chat syndrome.

TREATMENT

OTHER INTERVENTIONS

- Early intervention education; physical, language, occupational therapy
- Associated condition treatment (e.g. heart defect repair)

WILLIAMS SYNDROME

osms.it/williams-syndrome

PATHOLOGY & CAUSES

- **Chromosomal deletion syndrome:** affects most organ systems
 - AKA Williams–Beuren syndrome
- 26–28 genes involved
- **Inheritance pattern:** sporadic (mutation during gamete formation)

CAUSES

- Hemizygous **microdeletion in long arm of chromosome 7 (7q11.23)**
 - Most chromosomal breaks in medial, centromeric duplicons (gene clusters organized in low-copy repeat blocks)
- May include **elastin gene (ELN) deletion:** involved in supravalvular aortic stenosis

RISK FACTORS

- Parental genetic defect (e.g. Williams syndrome)

COMPLICATIONS

- **Hypercalcemia/hypercalciuria;** nephrocalcinosis; dysfunctional voiding; chronic kidney disease; urinary tract congenital anomalies; gastrointestinal conditions (e.g. chronic constipation, cholelithiasis); diabetes mellitus; diabetic nephropathy; progressive valvular stenosis; joint limitations; systemic **arterial stenosis** (esp. **supravalvular aortic stenosis**); hypothyroidism; type I Chiari malformation (cerebellar tonsils extend to foramen magnum); recurrent otitis media

SIGNS & SYMPTOMS

- **“Elfin”/pixie-like facies:** flat nasal bridge, short upturned nose, long medial cleft, periorbital puffiness, full lips, wide mouth, broad forehead, medial eyebrow flare
 - More distinctive with age
- Hoarse voice, high-tone sensorineural hearing loss, noise sensitivity (hyperacusis)
- Short stature
- **Dental:** small/abnormally shaped teeth, malocclusion
- **Psychiatric:** friendly, “cocktail party” personality; cognitive impairment; weak visuospatial/visuomotor skills; strong language skills; development delay; anxiety, phobias; obsessive-compulsive traits
- **Neurologic:** hyperreflexia; clonus; extrapyramidal signs (e.g. tremor, bradykinesia, dystonia); cerebellar signs (e.g. incoordination)
- **Ocular:** strabismus, amblyopia
- **Gastrointestinal:** constipation, gastroesophageal reflux, rectal prolapse
- Hypertension
- **Hypercalcemia:** irritability, ↓ appetite, constipation, hypotonia

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound, echocardiogram

- Urinary tract abnormalities (e.g. bladder diverticula, renal aplasia)
- **Cardiovascular:** supraventricular aortic stenosis, “hourglass” aorta, left ventricular hypertrophy (occasionally)

LAB RESULTS

- **Lab tests:** altered thyroid function, hypercalcemia, hypercalciuria, ↑ serum creatinine
- **Cytogenetic tests:** FISH
- Comparative genomic hybridization

OTHER DIAGNOSTICS

- **Audiologic tests:** high-tone sensorineural hearing loss

TREATMENT

OTHER INTERVENTIONS

- **Early intervention education:** physical, language, occupational therapy
- **Associated condition treatment:** e.g. aortic stenosis surgical repair, hypertension treatment